Remarks

Reconsideration of the Application is respectfully requested.

Upon entry of the foregoing amendments, claims 43, 44, 46, 48-50, 52-57, 59-61, 63 and 64 are pending in the application, with claims 43 and 63 being the independent claims. Claims 43 and 63 have been amended. Claim 47 has been cancelled. Support for the amendments may be found throughout the as-filed specification. In particular, support for the amendments to claims 43 and 63 may be found, *inter alia*, at page 5, lines 9-10. Thus, no new matter has been added by way of the present amendments, and their entry is respectfully requested.

A request for continued examination (RCE) is being filed concurrently herewith. Therefore, the finality of the Office Action dated November 26, 2004 should be withdrawn, and the amendments and arguments set forth herein should be entered and considered. *See* 37 C.F.R. § 1.114(d).

Based on the above amendments and the following remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the outstanding rejections.

I. Summary of the Office Action

In the Office Action dated November 26, 2004, the Examiner made one objection to the specification and three rejections to the claims. Applicant respectfully offers the following remarks to overcome the objection and rejections.

II. Objection to the Specification

At pages 2-3, paragraph 1 of the Office Action, the Examiner objects to the specification, stating that the documents cited in the specification have been improperly incorporated by reference. Applicant respectfully traverses the objection.

The Examiner cites *Advanced Display Systems, Inc. v. Kent State University* for the proposition that "[t]o incorporate by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents." While the Court in *Advance Display Systems* did put forth such a standard with regard to incorporation by reference, a careful reading of the case *in toto* shows that the standard in *Advance Display Systems* is limited to an *anticipation determination* and is not the standard for a 35 U.S.C § 112, first paragraph determination. Specifically, the court in *Advance Display Systems* states that "Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication *in an anticipation determination*--by citing such material in a manner that make clear that the material is effectively part of the host document" (emphasis added). *Advanced Display Systems, Inc. v. Kent State University*, 54 USPQ2d 1673, 1679. However, the MPEP states in relevant part:

> [M]ere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure by 35 U.S.C. § 112, first paragraph. *In re Seversky*, 474 F.2d 671, 171 USPQ 144 (CCPA 1973)... Particular attention should be directed to specific portions of the reference document where the subject matter being incorporated may be found. MPEP § 608.01(p).

Thus, the standard for a proper incorporation by reference put forth in *Advance Display Systems*, which is limited to an anticipation determination, and the standard set forth in the MPEP regarding 35 U.S.C § 112, first paragraph, are distinct and separate standards. As such, the Examiner is in error when citing *Advance Display Systems* for the proper standard in determining whether an incorporation by reference is proper for the purposes of 35 U.S.C § 112, first paragraph.

In addition, the MPEP notes a distinction between "essential material," that which is necessary to (1) describe the invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode, and "non-essential subject matter," which is subject matter referred to for purposes of indication the background of the invention or illustrating the state of the art. MPEP § 608.01(p). Thus, different types of subject matter have distinct incorporation by reference requirements. The Examiner has failed to indicate what type of material is the basis for the present objection.

Accordingly, it is the Applicant's position that the Examiner' objection is in error because (1) the incorrect standard for a proper incorporation by reference has been asserted and (2) the Examiner has failed to particularly point out the specific material that is allegedly improperly incorporated by reference. Applicant respectfully requests that the Examiner either provide such specificity regarding the objection or withdraw the objection completely.

III. The Rejection of Claims 43, 44, 46-50, 52-57, 59-61, 63 and 64 Under 35 U.S.C. § 112, First Paragraph for Lack of Written Description Is Traversed

At page 3, paragraph 4 of the Office Action, the Examiner rejects claims 43, 44, 46-50, 52-57, 59-61, 63 and 64 for failing to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. The Examiner contends that claims 43 and 63 encompass compositions of a virtually limitless range of sizes, and that the specification fails to support such a range of sizes. Applicant respectfully traverses this rejection and reiterates and incorporates by reference the remarks made in the Applicant's previous replies concerning this rejection. Applicant also wishes to provide the additional following remarks.

At the outset, Applicant notes that independent claims 43 and 63, as currently presented, recite, in relevant part, "A composition consisting essentially of a plurality of double-stranded DNA fragments ranging in length *from about 25 kb to about 100 bases...*" Thus, the claimed invention does not relate to "compositions *of a virtually limitless range* of sizes."

The written description requirement of 35 U.S.C. § 112, first paragraph, is fully satisfied for the subject matter of the present claims. Applicant asserts that the claimed invention is sufficiently described in the disclosure such as to reasonably convey to one skilled in the relevant art that Applicant had possession of the claimed invention at the time the application was filed. This is illustrated throughout the specification and the examples. In particular, Applicant provides extensive disclosure of DNA fragment sizes (see the paragraphs bridging pages 4-5 and 5-6, as well as pages 8-10 of the specification), various sources for the DNA (see pages 7, 8, 10, 12), as well as particular exemplified embodiments in the Examples. Further, as noted by the Examiner at page 8,

paragraph 12 of the Office Action, "the various pages [4-6 and 8-10 of the specification] *do [t]each with detail as to possible increments between bands, as well as the number of copies of a base pair sequence that may be present in a given band...*" (emphasis added). Moreover, Applicant provides specific disclosure of DNA fragment sizes "ranging from *about 25 kb to about 100 bp...*" as required by the present claims. Specification at page 5, lines 9-10. Thus, Applicant provides not only a comprehensive description of the subject matter of the present invention but provides *ipsis verbis* written description of the subject matter of the present claims.

Accordingly, present claims 43, 44, 46, 48-50, 52-57, 59-61, 63 and 64 are based upon an adequate written description and the written description requirement of 35 U.S.C. § 112, first paragraph, is fully satisfied. Applicant respectfully requests that this rejection be reconsidered and withdrawn.

IV. Rejections under 35 U.S.C. § 103

A. The Rejection of Claims 43, 44, 46-50, 52-56, 59-60, 63 and 64 Under 35 U.S.C. § 103(a) As Being Unpatentable Over Life Technologies Catalogue (1995-1996) Is Traversed

At page 9, paragraph 16 of the Office Action, the Examiner rejects claims 43, 44, 46-50, 52-56, 59-60, 63 and 64 under 35 U.S.C. § 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996). The Examiner contends that it would have been obvious to one of ordinary skill in the art to have developed any of a variety of DNA ladders for use in an electrophoresis assay and to have adjusted the relative concentrations of the bands such that the intensities of any one or all of the bands was the same or more intense than others. Applicant respectfully traverses this rejection and

reiterates and incorporates by reference the remarks made in the Applicant's previous replies concerning this rejection. Applicant also wishes to provide the additional following remarks.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and/or knowledge available to one of skill in the art would have led that individual to arrive at the claimed invention. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988).

The present independent claims require a composition consisting essentially of "a plurality of double-stranded DNA fragments ranging in length from about 25 kb to about 100 bases," wherein the "fragments of each length are present in an amount that produces bands of substantially equal intensity after the composition is separated by gel electrophoresis and stained with a detectable label." Thus, the composition of the present invention, after being separated by gel electrophoresis and stained with a detectable label, produces a ladder of bands ranging from about 25 kb to about 100 bases in size, in which every band of the ladder is of substantially equal intensity relative to every other band within the ladder.

The Life Technologies Catalogue (1995-1996) does not disclose compositions consisting essentially of DNA fragments about 25 kb to about 100 kb, wherein fragments of each length are present in an amount that produces bands of substantially the same intensity when separated by gel electrophoresis and stained. A careful examination of the DNA ladders on pages 14-2 through 14-4 of the Life Technologies Catalogue reveals

that all of the listed DNA ladders display bands having substantial variance in intensity among the individual bands within each ladder.

Applicant also directs the Examiner's attention to Figure 2 and pages 21-22 of Applicant's application. Figure 2 illustrates the differences between the invention and various commercially available DNA ladders when analyzed by gel electrophoresis. Specifically, Lane 2 of Figure 2 contains the 1 kb ladder that is disclosed in Life Technologies Catalogue (1995-1996) at page 14-4 and which is specifically cited by the Examiner at page 9, paragraph 18 of the Office Action. Analysis of the 1 kb ladder shows that fragments of the 1kb ladder smaller than 1 kb appear substantially less intense than the 1018 bp increment band. In fact, the bands smaller than 1 kb are so much less intense than the other bands within the ladder that the bands are barely, if at all, visible. This is because the relative mass of each of these fragments (and thus the intensity of these bands when stained) decreases in proportion to its size. Thus, not every band of the 1 kb ladder is of substantially equal intensity relative to every other band within the 1 kb ladder. Additionally, Applicant directs the Examiner to the fact that the 1,636 bp and 500 bp bands stain more intensely than do other bands within the ladder.

Thus, the ladders in the Life Technologies Catalogue (1995-1996) do not teach or suggest the ladders of the current invention, which consist essentially of fragments ranging in length from about 25 kb to about 100 bases present in an amount that produces bands of substantially equal intensity after the composition is separated by gel electrophoresis and stained with a detectable label.

At page 12, paragraphs 29 and 30 of the Office Action, the Examiner states:

> It is further noted that there need be only two bands that are of "substantially equal intensity after the composition is separated by gel

> electrophoresis" (emphasis added). Accordingly, there need be present only two bands that are of "substantially equal intensity."
>
> * * *
>
> With the phrase "substantially equal intensity" not being defined, said phrase has been interpreted as allowing for significant variability between bands.

While it is true that the term "substantially equal intensity" is not specifically defined by the specification, the term "substantially equal relative mass" is defined by the specification. According to the specification, relative mass is substantially equal when the relative mass of each fragment is about the same to no more than 3 times the relative mass of another fragment (*see* Application at page 9). "By having substantially the same relative mass, the bands of the ladders or compositions of the invention have substantially equal intensity when staining after separation by gel electrophoresis" (*see* Application at page 5). Because the intensity of a band is directly proportional to its relative mass, it is clear that the term "substantially equal intensity" means that the fragment in question has no more than 3 times the intensity of another fragment.

As previously stated, the DNA ladders of the Life Technologies Catalogue (1995-1996) show bands of varying intensities that cannot be considered to be of "substantially equal intensity," as required by the present claims. This fact is demonstrated in Figure 2 of the present application. Lane 1 depicts a DNA ladder of the present invention, and lane 2 depicts a 1 Kb DNA Ladder that is commercially available from Life Technologies, Inc. The 1 Kb ladder differs from the invention in that the fragments smaller than 1 Kb appear <u>less</u> intense than the 1018 bp increment band. This is because the relative mass of each of these fragments (and thus the intensity of these bands when stained) decreases in proportion to its size. Also, the 1,636 bp band and the 500 bp band

stain more intensely than do other bands in the ladder (see Application at page 21, Figure 2 and Life Technologies Catalog (1995-1996), page 14-4, 1 Kb DNA ladder). Additionally, the Examiner has provided no proof that the ladders of the Life Technologies Catalogue (1995-1996) contain bands that fall within these definitions, or that it would have been obvious to one of ordinary skill in the art, after reading the Life Technologies Catalogue (1995-1996), to have developed the claimed invention.

Having established that the present claims are not anticipated by the disclosure of the Life Technologies Catalogue (1995-1996), the Examiner has attempted to cure the deficiencies of the Life Technologies Catalogue (1995-1996) by stating at page 9, paragraph 19:

> It would have been obvious to one o[f] ordinary skill in the art at the time of the invention was made to have developed any of a variety of DNA ladders for use in an electrophoresis assay and to have adjusted the relative concentrations of the bands such that the intensities of any one or all bands was the same or more intense than other as the ordinary artisan desired.

Thus, the Examiner has provided only his personal opinion that it would have been obvious to modify the disclosure of the Life Technologies Catalogue (1995-1996) to obtain the claimed invention and has provided no objective evidence to support such a position. However, it is well established that such broad conclusory statements regarding the teaching of a reference, standing alone, are not sufficient evidence to establish obviousness. *See In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). As such, the Examiner has not met his burden in establishing a *prima facie* case of obviousness. Applicant requests that if the Examiner has any additional personal knowledge which provides objective evidentiary support for the rejection, the Examiner

make such personal knowledge of record in the present matter via the submission of an affidavit as stipulated in 37 C.F.R. §1.104(d)(2).

Applicant also directs the Examiner's attention to the nature of the problem solved by the present invention. The present invention provides a DNA ladder which spans a broad size range and generates discrete bands which are clear and are of substantially equal intensity compared to each other when separated on a gel and stained. These features are not disclosed or suggested by the Life Technologies Catalogue (1995-1996). As such, the Life Technologies Catalogue (1995-1996) does not render the present invention obvious.

Accordingly, Applicant requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

B. The Rejection of Claims 57 and 61 Under 35 U.S.C. § 103(a) As Being Unpatentable Over Life Technologies Catalogue (1995-1996) in view of Lee Is Traversed

At page 10, paragraph 20 of the Office Action, the Examiner rejects claims 57 and 61 under 35 U.S.C. § 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996) as applied to claims 43, 44, 46-55, 52-56, 59-60, 63 and 64, and further in view of U.S. Pat. No. 5,268,568 to Lee. The Examiner contends that it would have been obvious to one of ordinary skill in the art to have modified the DNA ladders of the Life Technologies Catalogue (1995-1996) such that a dye comprising bromophenol blue was included, given its common usage in electrophoresis of DNA samples. The Examiner also contends that a kit comprising DNA ladders would have been an obvious

commercial expedient requiring little, if any, additional effort on the part of the ordinary artisan. Applicant respectfully traverses this rejection.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). What is needed is a reason, suggestion, or motivation in the prior art that would motivate one of ordinary skill to combine the cited references, and that would also suggest a reasonable likelihood of success in making or using the claimed invention as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Absent such suggestion and motivation, the cited references may not be properly combined to render the claimed invention obvious. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). In the present case, the Examiner's burden has not been satisfied.

The Examiner has provided no evidence of a suggestion or motivation to combine the Life Technologies Catalogue (1995-1996) and Lee. Thus, the Examiner has not met the burden required to establish a *prima facie* case of obviousness. Even if one skilled in the art were to combine the Life Technologies Catalogue (1995-1996) and Lee, this would not give the invention of claims 57 and 61. As detailed above, the Life Technologies Catalogue (1995-1996) fails to disclose or suggest "bands of substantially equal intensity," which is a required limitation of claims 57 and 61 based upon their

dependence on claim 43. Lee does not cure this defect in the Life Technologies Catalogue (1995-1996). Therefore a key limitation in claims 57 and 61 is not taught or suggested by the combination of the Life Technologies Catalogue (1995-1996) and Lee. Furthermore, because the claimed composition of the present application is non-obvious, the kit comprising the composition is also necessarily non-obvious.

In view of the foregoing remarks, Applicant respectfully requests that the rejections under 35 U.S.C. § 103(a) over the Life Technologies Catalogue (1995-1996) and Lee be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for immediate allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Robert W. Esmond

Robert W. Esmond
Attorney for Applicant
Registration No. 32,893

Date: Feb 28, 2005

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600